



## ATTACHMENT A Remarks

Claims 1-18 are pending in the present application with claims 7-13, 16 and 17 withdrawn from consideration. By this Amendment, Applicants have amended claim 15 and added new claim 18. Applicants respectfully submit that the present application is in condition for allowance based on the discussion which follows.

The Office Action notes that the Applicants have claimed priority as a continuation-in-part to PCT/FR00/00112 but there fails to be reference to this document or any other priority document in a cross-reference section of the specification. Contrary to the Examiner's allegation, a Preliminary Amendment filed on July 20, 2001 amended the specification by adding a new first paragraph which states, "This application is a continuation-in-part of international application number PCT/FR00/00112, filed January 19, 2000." Furthermore, the image file wrapper of the uspto.gov PAIR System includes the Preliminary Amendment and its attachment, labeled "miscellaneous incoming letter" of 7-20-2001. Accordingly, Applicants respectfully submit that the specification does provide cross-reference to the PCT application to which the present application is a continuation-in-part.

Claims 3-4 and 15 were rejected under 35 U.S.C. § 112, second paragraph, with claims 3 and 4 rejected for depending from a rejected claim, namely claim 1 rejected under 35 U.S.C. § 102(b), and claim 15 being rejected for being indefinite as to what a diagnostic system comprises.

With regard to the rejection of claims 3 and 4, Applicants respectfully submit that upon consideration of this Amendment, and in particular the discussion which follows,

the rejection to claim 1 under 35 U.S.C. § 102, should be withdrawn. Thus, claims 3 and 4 will not be indefinite as depending from a rejected claim.

With regard to the rejection of claim 15, Applicants respectfully submit that the amendment to claim 15 now renders the rejection now moot. Claim 15 (currently amended) recites that the diagnostic system contains at least one compound of general formula (1) and a substrate of APA, and optionally, appropriate means for detecting degradation of the substrate.

The amendment to claim 15 is entirely supported in the original disclosure, e.g., at original example 9 which describes that APA is titrated using Glu-NA (page 21, line 32), which is a synthetic substrate of APA (page 21, lines 26-27), in the presence of an inhibitor. Accordingly, no new matter has been entered.

APA is an ectopeptidase which degrades substrates having Asp or Glu in the N-terminal position (page 1, lines 10-12). Accordingly, the processing of Glu-NA is measured by assessing the quantity of NA produced. As shown in example 9, this is achieved by measuring the absorbance of the reaction mixture after successive addition of NaNO<sub>2</sub>, ammonium sulphamate and 1-naphtylethylene diamine.

Example 9 thus describes an example of APA substrate and appropriate detection means that may be used to detect and titrate APA.

Furthermore, other substrates are known in this art, which could be used in the detection system, such as one of the physiological substrates of APA, CCK8 and angiotensin II (page 12, lines 30-33).

Accordingly, the one skilled in the art would readily know that the detection of APA activity may be carried out using an APA substrate and means for detecting degradation of the substrate.

Thus Applicants respectfully submit that claim 15, as amended, does not add new matter and further satisfied the requirements of 35 U.S.C. § 112.

Claims 1-2, 5 and 14 were rejected under 35 U.S.C. § 102(b) as being anticipated by Godfrey et al (EP 0 181 644, hereinafter "Godfrey") and claim 6 was rejected under 35 U.S.C. § 103(a) as being obvious in view of Godfrey. The Examiner alleges that Godfrey teaches compounds of the genus comprising compounds of the general formula (I), as recited in claims 1 and 14, and include many of the side reacting or protecting groups recited in claims 2 and 5. With regard to claim 6, the Examiner alleges that Godfrey suggests the claimed compound.

Contrary to the Examiner's allegation, Godfrey fails to teach or suggest any compound of the general formula (I).

Godfrey does not disclose any compound that falls within the scope of formula (I). Furthermore there is no overlapping zone between the claimed formula (I) and the genus disclosed in this prior art. Indeed, according to the present invention, the group  $R_1$  necessarily includes a substituent selected from  $-COOH$ ,  $SO_3H$ ,  $PO_3H_2$  optionally substituted by a  $(-CH_2CH_2SCOR_5)$ , or a tetrazolyl group.

This group  $R_1$  is not disclosed nor suggested in Godfrey.

Hence, Godfrey does not teach a genus comprising the general formula (I). As a result, Godfrey does not affect the novelty of claims 1, 2, 5 and 14.

With regard to the rejection of claim 6, Godfrey provides no motivation or incentive for one of ordinary skill in the art to modify the limitations of the genus disclosed in this prior art to make the compound of general formula (I) nor the specific compounds of claim 6.

Based on the foregoing, the subject matter of claims 1, 2, 5, 6 and 14 is not anticipated nor made obvious by Godfrey. Accordingly, Applicants respectfully request that the 35 U.S.C. § 102(b) rejection of claims 1, 2, 5 and 14 and the § 103 rejection of claim 6 in view of Godfrey be withdrawn.

By this Amendment, Applicants have added new claim 18 specifically directed to the compound of claim 1 wherein the pentyl group that protects the SO<sub>3</sub>H group is a neopentyl group.

Support for claim 18 can be found in the specification as filed and thus does not constitute new matter. Specifically, example 1, step 2, discloses that the sulphonate is brought into the synthesis as a neopentyl diethylphosphonomethane sulphonate (page 15, line 29). Furthermore, the use of this protecting group is thoroughly described in the application. For instance, examples 2 to 8 all refer to the steps of the process detailed in example 1, and include in particular step 2.

Accordingly the one skilled in the art would readily know in view of the specification, that a specific pentyl protecting group can be a neopentyl group.

Finally, since claims 3, 4, and 15 were not subject to a prior art rejection, Applicants conclude that claims 3, 4, and 15 are indicated as being clear of the prior art.

In view of the foregoing, Applicants respectfully submit that the present amendments and arguments overcome all objections of record, and that the present application is in condition for immediate allowance. Such action is earnestly solicited.

**END OF REMARKS**